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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/555,574 | 10/23/2000 | Jean-Paul Behr | 0652.2090000 | 9271 |

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| EXAMINER |
|---|
| SCHMIDT, MARY M |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | 23 |

DATE MAILED: 06/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/555,574 | BEHR ET AL. | |
| | Examiner | Art Unit | |
| | Mary M. Schmidt | 1635 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 21 April 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *21 April 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☐ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,2,5-33,37-41,45,46,48 and 49*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 5. NOTE: The amendment filed 4/21/03 amends claims 1, 5 and 6 and adds new claim 49. This proposed amendment adds the following new limitation to claim 1: "wherein the cationic precursor molecules comprise: a) at least one functional group for binding to one or more other of said precursor molecules, wherein said functional groujp is a dimerizable or polymerizable functional group selected from the group consisting of thiols, acid hydrazides, aldehydes, amines, and ethylene residues that are suitably substituted to provide enamines upon reaction with an amine, b) at least one lipophilic residue, c) a non-toxic reciptient backbone, and d) a cationic group for binding to nucleic acid molecules" was previouly found in claims 3 and 4 as filed, but remains rejected for the reasons of record set forth in previous Office actions over the breath of species of functional group of any thiol, acid hydrazide, aldehyde, amine and ethylene as the cationic molecule in the transfection particles. The 35 U.S.C. 112, scope of enabment, remains since the transfection particles have specific functional language that must be taken into consideration (ie. the requirement that the cationic molecules are made by "condensing said one or more nucleic acid molecules with identical or different organic cationic precursor molecules without crosslinking any of said one or more nucleic acid molecules" and "by linking the precursor molecules to each other with one or more covalent bonds") and thus the claimed molecules as amended must capable of being made without crossinglinking, ie. by condensation with the nucleic acid molecules. The previously Office action on the merits taught the unpredictability in the art for making any such transfection particle.

On page 8 of the response applicants argue that only one recited use is needed to enable the claimed compounds and that applicants compositions "can be used for in vitro transfection which is a notoriously well known use." However, while it is true that there are many transfection agents known for in vitro transfection use in the prior art, they are distinguished from applicants claimed invention since applicants claimed invention requires that the transfection agents are not cross-linked in the process of making the claimed compositions. Furthermore, the 35 U.S.C. 112, rejection is a scope of enablement rejection, and the transfection particles that are demonstrated in the examples in the specification are considered enabled for transfection of nucleic acids in vitro. It is the breath of claimed transfection particles that is not considered enabled for one of skill in the art to make and use at the time the invention was made for the reasons set forth previously.

On page 9 of the response applicants argue that "because Applicants are not claiming a liposomal composition, any alleged unpredictability in the making of liposomal structures is irrelevant to the enablement inquiry. Applicants respectfully tranverse this aspect of the rejection and reiterate that the Examiner has not met her burden of demonstrating that the specification fails to enable how to make the full scope of the claimed inventions." This is not considered persuasive since applicant is denying that references containing information on the unpredictability of making lipid based transfection vehicles that are used for transporting nucleic acids are applicable to the instant claims which are also drawn to compositions that are lipid based compositions condensed with nucleic acids. Applicant further makes a comparison of the teachings of Zelphati et al. and applicants claimed invention and states that since applicants transfection particles are made by a different process, that they are distinct from the liposomes taught by Zelphati et al. However, applicant has not addressed the specifics of the rejection of record, which pointed out the unpredictability (from other references as well) in choosing agents that are able to form functional linkage between the lipophilic and the hydrophilic regions of the transfection particle. Despite which methods are used to link, cross-linking or condensation, the same issues arise for the ability of the transfection agents to pass through the cell membrane. The function of passing through the cell membrane is what defines the linked lipohilic and hydrophilic regions of the transfection particle as functional or not. Thus, since the references cited teach the unpredictability of forming such transfection particles having these basic moieties, the same as the istantly claimed transfection particles, applicants' arguments are not considered pursuasive.

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6/4/03